



PATENT  
Customer No. 22,852  
Attorney Docket No. 3806-0488-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: )  
 )  
Christian VISKOV ) Group Art Unit: 1653  
 )  
Application No.: 09/742,008 ) Examiner: Kam, C.  
 )  
Filed: December 22, 2000 )  
 )  
For: NOVEL PROCESS FOR )  
PREPARING CYCLOSPORIN )  
DERIVATIVES )

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**RESPONSE TO RESTRICTION REQUIREMENT**

In a restriction requirement dated June 25, 2003, the period for response to which is the subject of the concurrently filed Petition to Revive, the Examiner required restriction under 35 U.S.C. § 121 between the following groups:

Group I (claims 1-14 and 22-23, drawn to a process for preparing a polyanion for use as an intermediate in the preparation of a cyclosporin derivative, comprising treating a cyclosporin with a hexamethyldisilazane metal salt; or a process for preparing a cyclosporin derivative substituted at 3-position, comprising preparing the polyanion);

Group II (claims 15-16, drawn to a method for preventing or treating a retrovirus infection or an associated syndrome, comprising administering to a mammal a cyclosporin derivative defined in part 1-4 or 7 of claim 14);

Group III (claims 17 and 19-20, drawn to a method for treating a chronic inflammatory disease, an autoimmune disease or inflammation, comprising administering to a

mammal a cyclosporin derivative in part 5-6 or 8 of claim 14);

Group IV (claim 18, drawn to a method for preventing or treating an autoimmune disease or preventing rejection of a transplant organ, comprising administering to a mammal a cyclosporin derivative in part 6 or 8 of claim 14); and

Group V (claim 21, drawn to a method for treating schistosomiasis, filariasis, leishmaniasis, coccidioidomycosis, or malaria, comprising administering to a mammal a cyclosporin derivative in part 6 or 8 of claim 14).

Applicant elects to prosecute Group I, claims 1-14 and 22-23, drawn to a process for preparing a polyanion for use as an intermediate in the preparation of a cyclosporin derivative, comprising treating a cyclosporin with a hexamethyldisilazane metal salt; or a process for preparing a cyclosporin derivative substituted at 3-position, comprising preparing the polyanion; with traverse.

In traversing the restriction requirement, Applicant directs the Examiner's attention to M.P.E.P. § 803, which sets forth criteria for the Examiner to follow in making a proper requirement for restriction. The following passage is pertinent to the issue herein.

**CRITERIA FOR RESTRICTION BETWEEN  
PATENTABLY DISTINCT INVENTIONS**

There are two criteria for a proper requirement for restriction between patentably distinct inventions:

- (1) The inventions must be independent (see M.P.E.P. §§ 802.01, 806.04, 808.01) or distinct as claimed (see M.P.E.P. §§ 806.05-806.05(i)); and
- (2) There must be a serious burden on the Examiner if restriction is not required (see M.P.E.P. §§ 803.02, 806.04(a)-(i), 808.01(a), and 808.02).

In the present case, the Examiner has not shown that there would be a serious burden involved in examining Groups I-V, despite the statement that the inventions are distinct. Applicant respectfully submits that a search of Groups I-V would not be burdensome, as all of the method of use claims recite using a compound represented by formula I. As the Examiner points out, all five groups are classified in class 514, among others. Accordingly, a proper search for the subject matter of one group would necessarily overlap the search for the subject matter of the remaining groups. Thus, a search for the subject matter cited in all groups would not be burdensome.

The Examiner also required that Applicant "select one cyclosporin compound from claim 4 or claim 14 (or claim 23) with each R<sub>1</sub>, R<sub>2</sub>, R<sub>4</sub> to R<sub>11</sub>, and Z<sub>1</sub>, Z<sub>2</sub> and Z<sub>4</sub>-Z<sub>11</sub> defined." Applicant elects the compound of Example 1, [(R)-2-(N,N-dimethylamino)ethylthio-Sar]<sup>3</sup>-[4'-hydroxy-MeLeu]<sup>4</sup>-cyclosporin A. This corresponds to a compound of claim 4 wherein the substituents are as defined in group ii. That is, the radicals R<sub>1</sub>, R<sub>2</sub>, and R<sub>4</sub> to R<sub>11</sub>, and Z<sub>1</sub>, Z<sub>2</sub>, and Z<sub>4</sub> to Z<sub>11</sub> are defined as for cyclosporin A, with the exception of R<sub>4</sub> and Z<sub>4</sub>, which are defined so as to have, at the 4-position, the amino acid 4'-hydroxy-methylleucine.

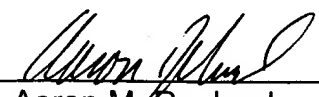
If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Dated: June 17, 2004

By: \_\_\_\_\_

  
Aaron M. Raphael  
Reg. No. 47,885